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10/520,745	08/22/2005	Colin Maurice Casimir	20050022.ORI	3261

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,745	CASIMIR, COLIN MAURICE	
	Examiner	Art Unit	
	Wu-Cheng Winston Shen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43-67* is/are pending in the application.

4a) Of the above claim(s) *49 and 57-67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-48 and 50-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response received on 03/09/2007 has been entered. Claims 1-42 were cancelled. Claims 43-67 are pending. Claim 43 was amended.

Claims 49 and 57-67 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

This application 10/520,745 filed on Aug. 22, 2005 is a 371 of PCT/GB03/03012 filed on 07/11/2003.

Status of claims: Claims 43-48 and 50-56 are currently under examination.

Claim Rejection – 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. The rejection of claim 43 and its dependent claims 44-48, and 50-56 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement because the claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is ***withdrawn*** because the combination the claim amendments and Applicant's arguments are found persuasive.

2. Claims 43-48 and 50-56 remained rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of making a retroviral particle, comprising providing a retroviral packaging cell that contains gag-pol genes, and produce envelope proteins, and nucleic acid sequences enabling replication, and transfecting the said retroviral packaging cell line with an expression vector comprising a nucleic acid encoding membrane bound human stem cell factor (SCF) operably linked to a eukaryotic promoter, wherein the resulting retroviral particle bear SCF on the surface of the retroviral particle that can target the retroviral particle to a megakaryoblastic leukemia cell line expressing c-kit, the receptor of SCF, does not reasonably provide enablement for any other non-retroviral particle having any other peptide binding moiety on the viral surface, wherein the said peptide binding moiety is a passenger peptide binding moiety that is encoded and expressed by any other non-retroviral viral packaging cell line and incorporated onto the surface of the said viral particle as a membrane bound protein during budding of the viral particles, wherein the said viral particles target to any other cells than megakaryoblastic leukemia cell line expressing c-kit, the receptor of SCF by any non-Env-receptor interactions between the peptide binding moiety on the surface of the viral particle and the interacting binding partner on the plasma membrane of the cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Previous rejection is ***maintained*** for the reasons of record advanced on pages 6-13 of the office action mailed on 09/05/06. It is noted that, upon further consideration, the Examiner has broadened the enabled scope encompassed by the claims. More specifically, limitations of the

enabled scope to hygromycin and diphtheria toxin as selectable markers, and EBV oriP along with EBAN-1 gene in a plasmid as an episome, have been withdrawn.

Applicant's Arguments

With respect to the aspect of the rejection regarding the breadth of the claims of a method of making a viral particle having a modified cell binding activity comprising non-retrovirus viral particles, Applicant argues that the claims are limited to viruses that bud from the packaging cell, therefore limiting them to viruses with lipid envelopes. Applicant argues that it is known to those in the art that all lipid-enveloped viruses are assembled and undergo budding from a lipid membrane in an almost identical manner. For example, the fundamental difference between retroviruses and other viruses is in the manner in which they replicate their genetic material, and not the mechanism in which they bud from host cells. Applicant further argues that the skilled person would know that different lipid enveloped viruses would behave in an almost identical manner in relation to both their mechanism of budding and the incorporation of proteins as passengers into their envelope. Any minor changes to the methods that were required in order to adapt the use for non-retroviral vectors would be only of a routine nature to the skilled person that works with the particular virus that will be used. As further support, Applicant provides an excerpt from a Virology textbook that describes the assembly of enveloped viruses, in which the process of assembly and budding is described and shown, to be very similar in different viruses at pages 84-85 is attached to this paper as Exhibit A. In this regard, Applicant indicates that the inventor is aware that further data also may be available in the literature.

Response to Applicant's Arguments

Applicant's arguments filed 03/09/2007 have been fully considered but they are not persuasive because of the reasons discussed below.

The Examiner acknowledges and agrees with the Applicant that budding processes of enveloped viruses are largely similar. However, the key issue under consideration of instant application regarding enablement support is the claimed method of altering cell binding activity (i.e. viral tropism) of a given viral particle by introduction of a nucleic acid sequence encoding a passenger peptide binding moiety, which is expressed as an component of the envelope of the said viral particle and can be recognized by the receptor of the said passenger peptide binding moiety, thereby changing the spectrum of cells infected by the said viral particle as compared to that of the viral particle without being introduced with a nucleic acid sequence encoding a passenger peptide binding moiety. It is not the budding process by itself that renders the claimed invention not enabled, rather it is the combination of multiple factors as a whole that a skilled person in the art cannot make and use the claimed invention commensurate to the scope of the invention. The issues contributing to the lack of predictability revealed in the prior arts and identified in the Non-Final rejection mailed on 09/05/2006 include (i) the size of passenger peptide binding moiety that can be expressed from and incorporated into a given viral genome, (ii) viral tropism determined by contacts between viruses and cell occur outside of the *bona fide* Env-receptor interaction, (iii) potential immune and inflammation responses as a result of introduced passenger peptide binding moiety and cell-derived components being concentrated along with viral vector particle, (iv) cross interaction between a passenger peptide binding

moiety and a receptor affecting recited altered tropism of a viral particle, a process involving the topology and expressed levels of the introduced passenger peptide binding moiety in the viral envelope and the topology and expressed levels of its corresponding receptor(s) present on the cell surface under a given growth condition. As discussed in the rejection under written description, the specification only discloses mb-SCF (membrane bound stem cell factor) introduced to be a envelope protein of a retroviral particle that can infect a human megakaryoblastic leukemia cell line that express a c-kit receptor, the receptor of mb-SCF. No specific direction and guidance is given regarding how the methods used for expressing mb-SCF can be modified to express any peptide binding moiety in any packaging cell line, for instance, the size limitation for and the control over expressing a given peptide binding moiety of interest in any viral packaging cell line would require undue experimentation for an skilled person in the art to make and use the claimed invention.

In conclusion, the specification as filed fails to provide any specific guidance and/or working examples, regarding non-retroviral particles. The specification also fails to direct the skilled artisan to any teachings on the relationship between the control of the expression level of a passenger peptide binding moiety and its incorporation into viral particles, and how this relationship affects the infectivity the viral particles to specific target cells, which would allow one of skill in the art to make and use the claimed invention without undue experimentation. In view of the state of the art, the unpredictability in the art, and the lack of guidance and working examples in the specification, one of skill in the art would have to perform undue experimentation to practice the breadth of the claimed invention. It is noted that Applicant failed to address other aspects of the enablement rejection except non-retroviral vector. Therefore, the

rejection with respect to the interactions between pseudotyped viral particle and cells expressing receptors for the pseudotyped polypeptide present on the viral particle, and the non-Env-receptor interactions involved in determination of viral tropism are maintained for reasons of the record.

Claim Rejection - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

3. Claims 43-48 and 50-56 are *newly* rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. *This rejection is necessitated by the claim amendments.*

The amended claim 43 recites, "wherein the passenger peptide binding moiety is other than a chimeric or fusion protein", which fails to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear what is encompassed by the phrase "*passenger* peptide-binding moiety" in term of the relationship of the protein coding sequences between the introduced nucleic acid encoding a passenger peptide-binding moiety and the viral endogenous nucleic acid encoding the gag-pol envelope, relative to the position of one promoter or multiple promoters in the modified viral genome. In other words, when peptide-binding moiety is not part of a fusion envelope protein, it is not clear in what sense the peptide-binding moiety is considered as a passenger, and by what molecular characteristics the recited passenger peptide-binding moiety can become part of the viral envelope.

Claim Rejection – 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 43-48 and 54- 56 rejected under 35 U.S.C. 102(b) as being anticipated by Jiang et al. (Jiang et al, Cell-type-specific gene transfer into human cells with retroviral vectors that display single-chain antibodies. *J Virol.* 72(12): 10148-56, 1998) are ***withdrawn*** because claim 43 has been amended.

The amended claim 43 recites a new limitation "wherein the passenger peptide binding moiety is other than a chimeric or fusion protein. In this regard, Jiang et al. teach single-chain antibodies (scAs), as part of a *fusion protein* with envelope, directed against a carcinoembryonic antigen (CEA)-cross-reacting cell surface protein.

5. Claims 43-46 and 54-56 are *newly* rejected under 35 U.S.C. 102(b) as being anticipated by Soong et al. (Soong et al., Molecular breeding of viruses. 25(4): 436-9, 2000). *This rejection is necessitated by the claim amendments of claim 43.*

Soong et al. teach a method molecular breeding of viruses, including retrovirus, with altered tropism without involving generation of fused viral envelope protein. Specifically, Soong et al. teach *in vitro* process of DNA shuffling (molecular breeding) mimics this mechanism on a

vastly parallel and accelerated scale. Multiple homologous parental sequences are recombined in parallel, leading to a diverse library of complex recombinants from which desired improvements can be selected. Different proteins and enzymes have been improved using DNA shuffling. Soong et al. performed the first application of molecular breeding to viruses. A single round of shuffling envelope sequences from six murine leukaemia viruses (MLV) followed by selection yielded a clone with a completely *new tropism* for Chinese Hamster Ovary (CHOK1) cells (See abstract, Figure 3, Soong et al., 2000).

It is noted that the limitation "nucleic acid encoding the passenger peptide binding moiety" recited in step (ii) of claim 43 reads on the viral nucleic acid encoding envelope protein during the molecular breeding process taught by Soong et al. Moreover, the method taught by Soong et al. doesn't involve chimeric or fusion envelope proteins. Instead, the altered tropism is a result of accelerated evolution of existing viral envelope proteins through recombination.

Thus, Soong et al. clearly anticipates claims 43-46 and 54-56 of instant application.

Claim Rejection – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The rejection of claim 51 under 35 U.S.C. 103(a) as being unpatentable over Jiang et al. (Jiang et al, *J Virol.* 72(12): 10148-56, 1998) in view of Dropulic et al. (U.S. patent No. 6,114,141, issued Sep. 5, 2000) is ***withdrawn*** because claim 43 has been amended.

The amended claim 43, from which claim 51 depends, recites a new limitation "wherein the passenger peptide binding moiety is other than a chimeric or fusion protein. In this regard, Jiang et al. teach single-chain antibodies (scAs), as part of a *fusion protein* with envelope, directed against a carcinoembryonic antigen (CEA)-cross-reacting cell surface protein.

7. The rejection of claims 52-53 under 35 U.S.C. 103(a) as being unpatentable over Jiang et al. (Jiang et al, *J Virol.* 72(12): 10148-56, 1998) in view of Guber et al. (U.S. patent No. 569,177, issued Nov. 25, 1997) is ***withdrawn*** because claim 43 has been amended.

The amended claim 43, from which claim 52 depends recites a new limitation "wherein the passenger peptide binding moiety is other than a chimeric or fusion protein. In this regard, Jiang et al. teach single-chain antibodies (scAs), as part of a *fusion protein* with envelope, directed against a carcinoembryonic antigen (CEA)-cross-reacting cell surface protein.

8. Claims 43, 48, 50 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soong et al. (Soong et al., Molecular breeding of viruses. *Nature* 25(4): 436-9, 2000) taken with Dropulic et al. (U.S. patent No. 6,114,141, issued Sep. 5, 2000; listed in the PTO-892 in Non-Final rejection mailed on 09/05/2006). *This rejection is necessitated by the claim amendments of claim 43.*

Soong et al. teach a method molecular breeding of viruses, including retrovirus, with altered tropism without involving generation of fused viral envelope protein. Specifically, Soong et al. teach *in vitro* process of DNA shuffling (molecular breeding) mimics this mechanism on a vastly parallel and accelerated scale. Multiple homologous parental sequences are recombined in parallel, leading to a diverse library of complex recombinants from which desired improvements can be selected. Different proteins and enzymes have been improved using DNA shuffling. Soong et al. performed the first application of molecular breeding to viruses. A single round of shuffling envelope sequences from six murine leukaemia viruses (MLV) followed by selection yielded a clone with a completely *new tropism* for Chinese Hamster Ovary (CHOK1) cells (See abstract, Figure 3, Soong et al., 2000).

It is noted that the limitation "nucleic acid encoding the passenger peptide binding moiety" recited in step (ii) of claim 43 reads on the viral nucleic acid encoding envelope protein during the molecular breeding process taught by Soong et al. Moreover, the method taught by Soong et al. doesn't involve chimeric or fusion envelope proteins. Instead, the altered tropism is a result of accelerated evolution of existing viral envelope proteins through recombination.

However, Soong et al., do not teach additional nucleic acid which can express any one of the bioactive agent selected from ricin, tumor necrosis factor, interleukin-2 (a cytokine), interferon-gamma, ribonuclease, deoxyribonuclease, pseudomonas exotoxin A and caspase.

With regard to claim 43, 48, 50 and 51, Dropulic et al. teach methods to express genes from viral vectors (See title and abstract). Specifically, Dropulic et al. teach the expression of antiviral agent including a cytokine, a single-chain antibody, a cellular antigen or receptor (See claims 4 and 21).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Soong et al. on the method of generating a virus with altered tropism and the teachings of Dropulic et al. on expressing a cytokine (interleukine-2) from a viral vector as taught by Dropulic et al. to achieve the claim 51 of instant application on a method of making a viral particle having a modified cell binding activity and also expressing a bioactive agent including interleukin-2.

One having ordinary skill in the art would have been motivated to modify the retroviral vector by the teachings of Soong et al. to express antiviral agent interleukin-2 by the teachings of Dropulic et al. to achieve the goal of site specific delivery of interleukin as an antiviral agent via the selection of altered tropism of viral particle.

There would have been a reasonable expectation of success given (1) the generation of viral particle with altered tropism resulting from accelerated evolution of envelope genes by the teachings of Soong et al., and (2) the expression of a cytokine from a viral vector by the teachings of Dropulic et al.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

9. Claims 43, 48, 52 and 53 are *newly* rejected under 35 U.S.C. 103(a) as being unpatentable over Soong et al. (Soong et al., Molecular breeding of viruses. 25(4): 436-9, 2000) taken with Guber et al. (U.S. patent No. 569,177, issued Nov. 25, 1997; listed in the PTO-892 in Non-Final rejection mailed on 09/05/2006). *This rejection is necessitated by the claim amendments of claim 43.*

Soong et al. teach a method molecular breeding of viruses, including retrovirus, with altered tropism without involving generation of fused viral envelope protein. Specifically, Soong et al. teach *in vitro* process of DNA shuffling (molecular breeding) mimics this mechanism on a vastly parallel and accelerated scale. Multiple homologous parental sequences are recombined in parallel, leading to a diverse library of complex recombinants from which desired improvements can be selected. Different proteins and enzymes have been improved using DNA shuffling. Soong et al. performed the first application of molecular breeding to viruses. A single round of shuffling envelope sequences from six murine leukaemia viruses (MLV) followed by selection yielded a clone with a completely *new tropism* for Chinese Hamster Ovary (CHOK1) cells (See abstract, Figure 3, Soong et al., 2000).

It is noted that the limitation "nucleic acid encoding the passenger peptide binding moiety" recited in step (ii) of claim 43 reads on the viral nucleic acid encoding envelope protein during the molecular breeding process taught by Soong et al. Moreover, the method taught by Soong et al. doesn't involve chimeric or fusion envelope proteins. Instead, the altered tropism is a result of accelerated evolution of existing viral envelope proteins through recombination.

However, Soong et al., do not teach additional nucleic acid which can express any one of the bioactive agent, which is an enzyme, including thymidine kinase and cytosine deaminase, capable of converting a relatively non-toxic pro-drug into a cytotoxic drug.

With regard to claims 43, 48, and 52-53, Guber et al. teach recombinant retroviruses expressing a protein that converts a pro-drug into a cytotoxic agent (See title and abstract). Specifically, Guber et al. teach the expression of a nucleoside kinase thymidine kinase (See

claims 6-8, 22-23) that converts a purine-based or pyridimine-based drug with little or no cytotoxicity into a cytotoxic drug (See claim 5)

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Soong et al. on the method of generating a virus with altered tropism and the teachings of Guber et al. to express a thymidine kinase that converts a pro-drug into a cytotoxic drug to achieve the claims 52 and 53 of instant application regarding a method of making a viral particle having a modified cell binding activity and also expressing a bioactive agent such as thymidine kinase capable of converting a relatively non-toxic pro-drug into a cytotoxic drug.

One having ordinary skill in the art would have been motivated to modify the retroviral vector by the teachings of Soong et al. to express thymidine kinase by the teachings of Guber et al. to achieve the goal of site specific delivery of thymidine kinase to a desired cell target for converting a pro-drug into a cytotoxic drug via the binding specificity of altered tropism of virus as taught by Soong et al.

There would have been a reasonable expectation of success given (1) the generation of viral particle with altered tropism resulting from accelerated evolution of envelope genes by the teachings of Soong et al., and (2) the expression of thymidine kinase converting a pro-drug into a cytotoxic drug from a recombinant retroviral vector by the teachings of Guber et al.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

10. Claims 43 and 47 are *newly* rejected under 35 U.S.C. 103(a) as being unpatentable over Soong et al. (Soong et al., Molecular breeding of viruses. 25(4): 436-9, 2000) taken with Yajima

et al. (Retroviral vector targeting human cells via c-Kit-stem cell factor interaction. *Hum Gene Ther.* 9(6): 779-87, 1998; listed as the last reference in the IDS filed on 05/04/2007). *This rejection is necessitated by the claim amendments of claim 43.*

Soong et al. teach a method molecular breeding of viruses, including retrovirus, with altered tropism without involving generation of fused viral envelope protein. Specifically, Soong et al. teach *in vitro* process of DNA shuffling (molecular breeding) mimics this mechanism on a vastly parallel and accelerated scale. Multiple homologous parental sequences are recombined in parallel, leading to a diverse library of complex recombinants from which desired improvements can be selected. Different proteins and enzymes have been improved using DNA shuffling. Soong et al. performed the first application of molecular breeding to viruses. A single round of shuffling envelope sequences from six murine leukaemia viruses (MLV) followed by selection yielded a clone with a completely *new tropism* for Chinese Hamster Ovary (CHOK1) cells (See abstract, Figure 3, Soong et al., 2000).

It is noted that the limitation "nucleic acid encoding the passenger peptide binding moiety" recited in step (ii) of claim 43 reads on the viral nucleic acid encoding envelope protein during the molecular breeding process taught by Soong et al. Moreover, the method taught by Soong et al. doesn't involve chimeric or fusion envelope proteins. Instead, the altered tropism is a result of accelerated evolution of existing viral envelope proteins through recombination.

However, Soong et al., do not teach the introduced peptide binding moiety being membrane bound stem cell factor as recited in claim 47 of instant application.

With regard to claims 43 and 47, Yajima et al. teach engineering a recombinant retroviral vector that can target human cells expressing a c-Kit receptor via a ligand-receptor interaction. Specifically, the lined is a stem cell factor and the receptor is c-Kit receptor.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Soong et al. on the method of generating a virus with altered tropism and the teachings of Yajima et al. on a recombinant retroviral vector that can target human cells expressing a c-Kit receptor via a ligand-receptor interaction to achieve the claims 42 and 47 of instant application regarding a method of making a viral particle having a modified cell binding activity and expressing a membrane bound stem cell factor.

One having ordinary skill in the art would have been motivated to modify the retroviral vector by the teachings of Soong et al. and express stem cell factor by the teachings of Yajima et al. to achieve the goal of targeted gene transfer into stem cell, such as hematopoietic stem cells, by retroviral vectors to facilitate the development of in vivo strategies for stem cell gene therapy via the binding specificity of altered tropism of virus as taught by Soong et al.

There would have been a reasonable expectation of success given (1) the generation of viral particle with altered tropism resulting from accelerated evolution of envelope genes by the teachings of Soong et al., and (2) a recombinant retroviral vector that can target human cells expressing a c-Kit receptor via a ligand (SCF)-receptor (C-Kit) interaction by the teachings of Yajima et al.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Conclusion

11. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent

examiner, Peter Paras, can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Wu-Cheng Winston Shen, Ph. D.
Patent Examiner
Art Unit 1632